Strain-Dependent Susceptability to Transplacentally-Induced Murine Lung Tumors

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Previously, our laboratory demonstrated that fetal mice are more sensitive to *in utero* exposure to the polycyclic hydrocarbon, 3-methylcholanthrene (MC), than are adults, and that resistant strains had a high incidence of lung tumors 12 months after transplacental exposure to MC. We compared the effects of *in utero* treatment with MC on lung tumor induction in the offspring of intermediately susceptible Balb/c (Bc), resistant C57BL/6 (B6), and reciprocal crosses between the two strains. Pregnant mice were treated with 45 mg/kg of MC on day 17 of gestation and tumor incidence and multiplicity determined in the offspring 12-18 months after birth. Bc, B6Bc, and BcB6 mice exhibited a 100% tumor incidence whereas the resistant B6 mice had an incidence of 11%. B6 mice exhibited 4 small nodules after 18 months, whereas Bc mice rarely survived beyond 14 months and BcB6 and B6Bc mice survived to approximately 16 months. Bc, B6Bc, and BcB6 mice exhibited significant tumor involvement in the lungs; in many cases multiple tumors coalesced into single large masses with the majority of lesions classified as adenocarcinomas. Counting only lesions that were discrete, individual nodules, tumor multiplicities in Balb, B6Bc, BcB6, and B6 mice were 5.8 ± 3.7, 5.0 ± 3.3, 4.9 ± 3.6, and <0.1, respectively. These results suggest that, similar to adults, crosses between susceptible and resistant strains results in a susceptible phenotype for lung cancer. We are currently examining differences in MC metabolism, DNA adduct levels and repair, and mutations in Ki-*ras* as possible mechanistic factors mediating strain susceptibility to lung carcinogens. These studies highlight the important interactions between genetic and environmental factors in determining individual susceptibility to environmental toxicants during development.

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